THE PHYSIOLOGICAL ACTION OF HYOSCYAMINE.

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(*Continued.*)

THE action of the alkaloid on the temperature and pupil it was thought best to study on man; this also gave us the opportunity of studying the effect on the respiration, pulse, etc. I shall first give the observations on the pulse, temperature, and respiration; another series were made specially to study its effect on the pupil.

These observations were made in conjunction with my assistant, Dr. G. N. Ferris.

OBSERVATION I.

E—— J——.

Dementia, terminal.

Patient small of stature, but fairly developed. Health good.

	A. M.	
Pulse 80. Resp. 26. Axilla 98⅗°. Temp. rectum 99⅕°. Pupils normal.	10	Patient is put in bed some minutes before observations are made. Lies quietly. Given ⅙ gr. H. by mouth.
Pulse 80. Resp. 26. Axilla 98⅗°. Temp. rectum 99°. Pupils normal.	10.45	No change noticeable in patient.

	A. M.	
Pulse 96. Resp. 20. Axilla $98\frac{2}{5}^\circ$. Temp. rectum $98\frac{4}{5}^\circ$. Pupils a little larger.	11.30	Patient quiet, but not disposed to sleep.
	P. M.	
Pulse 92. Resp. 20. Axilla 98°. Temp. rectum $98\frac{2}{5}^\circ$. Pupils large.	12.30	Sleeping but rouses easily. While observations are being made, restless, talking incoherently to himself, yawns. Conjunctiva injected. Face flushed.
Pulse 80. Resp. 20. Axilla $97\frac{4}{5}^\circ$. Temp. rectum $98\frac{2}{5}^\circ$. Pupils large.	2	Has been sleeping since last note. Lies quietly. Yawns frequently. Mouth a little dry. Conjunctiva red.
Pulse 72. Resp. 22. Axilla $97\frac{3}{5}^\circ$. Temp. rectum $98\frac{2}{5}^\circ$. Pupils smaller.	3.20	Does not seem so sleepy, but remains quietly in bed.
Pulse 72. Resp. 22. Axilla $98\frac{3}{5}^\circ$. Temp. rectum $99\frac{1}{5}^\circ$. Pupils still dilated.	4.45	Effect of drug seems to have passed away. Patient quite lively, but complains of some headache.
Pulse 80. Resp. 24. Axilla $98\frac{1}{5}^\circ$. Temp. rectum $99\frac{1}{5}^\circ$. Pupils still dilated.	6.30	Ate his supper. Seems as usual. Quite talkative. Pupil contracts by candle light.

OBSERVATION 2.

L—— B——.

Dementia.

	A. M.	
Pulse 84. Resp. 28. Axilla $97\frac{2}{5}^\circ$. Temp. rectum $99\frac{2}{5}^\circ$. Pupils rather large.	10.45	Patient has been walking around restlessly, laughing and talking to himself. When put to bed, lies quietly and makes no resistance to observations.

11 A.M., given $\frac{1}{6}$ gr. hyoscyamine by mouth.

	A. M.	
Pulse 68. Resp. 28. Axilla $98\frac{3}{5}^\circ$. Temp. rectum $99\frac{2}{5}^\circ$. Pupils the same.	11.30	Patient lies quietly in bed, does not seem sleepy, laughs to himself.

	P. M.	
Pulse 84. Resp. 28. Axilla 98⅖°. Temp. rectum 99⅖°. Pupils the same.	12.30	Since last visit patient got up and dressed, but was put to bed again by nurse. Lies in a quiet state, looks around him, and then pretends to sleep.
Pulse 88. Resp. 22. Axilla 98⅖°. Temp. rectum 99⅕°. Pupils dilated.	1.30	Patient appears drowsy, but opens his eyes when spoken to. Conjunctiva injected; face flushed.
Pulse 88. Resp. 24. Axilla 98⅕°. Temp. rectum 99⅕°. Pupils dilated.	3.15	Is still very drowsy, but wakens easily. Conjunctiva still red.
Pulse 100. Resp. 24. Temp. axilla 98⅗°. Pupils dilated.	6	Pulse though frequent is regular. Patient wide awake.

OBSERVATION 3.

J—— K——.

Chronic Mania.

	A. M.	
Pulse 54. Resp. 16. Axilla 97⅘°. Temp. rectum 99⅖°. Pupils normal.	11	Patient is frequently excited. To-day is talkative and noisy. Is in good physical health. Given ⅙ grain hyoscyamine by mouth.
Pulse 76. Resp. 14. Axilla 97⅕°. Temp. rectum 98⅖°. Pupils dilated.	11.45	Respiration blowing. Sleeping soundly. Yawns frequently. Conjunctiva injected.
	P. M.	
Pulse 68. Resp. 16. Axilla 97⅗°. Temp. rectum 98⅖°.	1	Sleeping quietly and snoring. Does not notice temperature taking.
Pulse 52. Resp. 14. Axilla 97⅖°. Temp. rectum. 98⅘°. Pupils dilated.	2.45	Sleep natural. Pupils are dilated but respond to light; smaller during sleep.
Pulse 50. Resp. 16. Axilla 97⅖°. Temp. rectum 99°. Pupils dilated.	4.45.	Still sleepy, but rouses easily and eats his supper.

7 P. M., effect has quite passed off. Patient very talkative and wide awake.

OBSERVATION 4.

J—— B——.

Dementia.

	A. M.	
Pulse 88. Resp. 24. Axilla 98°. Temp. rectum 99°. Pupils small.	11.15.	Patient quiet. Stands for some time in one position. Circulation poor, hands very blue. Given ⅛ grain hyoscyamus hypodermically.
Pulse 68.	11.20.	
Pulse 80. Resp. 22.	11.25	
Pulse 120.	11.35	Unsteady, beats strongly and regularly, then rapidly and weak.
Temp. axilla 98°.	11.30.	
Temp. rectum 99°.	11.37.	
Pulse 120. Resp. 18. Pupils a little dilated.	11.40.	Patient asleep, yawns. Commences the peculiar shaking noticed the other day.
	P. M.	
Temp. axilla 98⅕°.	12.30.	Very difficult to count pulse and respirations, as patient rubs his hands, slaps his hands and face, rolls around. Capillary circulation much improved.
Resp. 22. Temp. rectum 99°. Pupils large.	12.35.	
Pulse 96. Resp. 20. Axilla 99°. Temp. rectum 99⅖°.	2.00.	Partially asleep. Is agitated during observations as before, but not so markedly.
Pulse 68. Resp. 24. Axilla 98°. Temp. rectum 99⅕°. Pupils large and respond to light.	5	Patient has quite recovered. Wide awake, laughs in his stupid manner. Does not object to observations. Eats his supper.

OBSERVATION 5.

J—— B——.

Dementia.

	A. M.	General health fair. Capillary circulation poor. Patient restless, stupid and incoherent.
Pulse 84. Resp. 24. Axilla 98⅘°. Temp. rectum 99⅕°. Pupils normal.	10.20	Temperature taken after patient is in bed. Patient goes to bed quietly and makes no resistance to observations.

10.20 A. M., given ⅙ grain hyoscyamine by mouth.

Pulse 116. Resp. 16. Axilla 98⅗.° Temp. rectum 99⅕°. Pupils a little larger.	11	Conjunctiva slightly injected. Is found asleep, but rouses easily; when left quiet sleeps again.
Pulse 112. Resp. 18. Axilla 99⅖°. Temp. rectum 100°. Pupils dilated.	M. 12	Conjunctiva more injected. Very restless, hard to take observations, shakes all over, rubs his hands, shakes his head. Capillary circulation much improved.
Pulse 92. Resp. 16. Axilla 99°. Temp. rectum 99⅘°. Pupils dilated.	P. M. 1	Pulse rather compressible and difficult to count. Patient still restless and rolling around the bed.
Pulse 80. Resp. 20. Axilla 98⅕°. Temp. rectum 99⅕°. Pupils smaller.	2.15	Patient not so restless, allows observations to be taken easily. Laughs and seems nearer his usual condition. Mouth quite dry. Is given ⅙ grain H. by mouth.
Pulse 104. Resp. 16. Axilla 98⅕°. Temp. rectum 98⅘°. Pupils large.	3.00	Is found sitting on the side of bed looking very sleepy. Becomes restless while taking temperature. Conjunctiva not so red.
Pulse 88. Resp. 16. Axilla 98⅕°. Temp. rectum 99°. Pupils large.	4.15	Looks dazed, but is not disposed to sleep, is restless, rolls about bed, shakes his body and arms.
Pulse 80. Resp. 22. Axilla 98⅖°. Temp. rectum 99⅕°. Pupils still dilated.	5.45	Lies quietly in bed, but does not sleep. Refused his supper.

	P. M.	
Pulse 72. Resp. 20. Axilla $97\frac{4}{5}$°. Temp. rectum 99°. Pupils a little smaller.	6.45	Find him walking about the bedroom and chilly. When put in bed laughs and lies quietly. Mouth still very dry.

OBSERVATION 6.

A—— B——.

Chronic Mania.

	P. M.	
Pulse 92. Resp. 20. Axilla $97\frac{4}{5}$°. Temp. rectum $99\frac{4}{5}$°. Pupils normal.	3.06	Patient restless, noisy, moving about constantly.

At 3.25 P. M., given $\frac{1}{3}$ gr. hyoscyamine by mouth.

	P. M.	
Pulse 112. Resp. 17. Axilla 99°. Temp. rectum $100\frac{2}{5}$°.	4	Patient quieter but still restless, not disposed to sleep. No effect whatever on pupils.
Pulse 96. Resp. 20. Temp. axilla 99°. Pupils the same.	6	Patient in bed, still restless, going through all sorts of pantomimic movements. Pupils not affected in the least.

OBSERVATION 7.

J—— T——.

Chronic Mania.

	A. M.	
Pulse 100. Resp. 20. Temp. rectum $99\frac{1}{5}$°. Pupils rather large.	9.25	Very talkative, not violent at present, but tearing up clothing. Given $\frac{1}{3}$ gr. hyoscyamine by mouth.
Pulse 110. Resp. 18. Temp. rectum $99\frac{1}{5}$°. Pupils a little larger.	10.20	Still talkative. No sleep. No disturbance of motor apparatus. Given $\frac{1}{3}$ gr. hyoscyamine by mouth.
Pulse 116. Resp. 18. Temp. rectum $99\frac{1}{5}$°. Pupils dilated.	11.15	Respiration slightly labored. Patient quiet, not so talkative.
	P. M.	
Pulse 96. Resp. 16. Temp. rectum 99°. Pupils dilated.	12.20	Has not slept, but is drowsy. When roused sits up and talks. All his movements are slow. Can walk, but slowly.

OBSERVATION 8.

J—— T——.

Chronic Mania.

	P. M.	
Pulse 88. Resp. 14. Axilla 99⅕°. Temp. rectum 101°. Pupils slightly dilated.	3.55	Is in good health. Somewhat excited. Very talkative, incoherent. Given ½ gr. hyoscyamine by mouth.
Pulse 92. Resp. 20. Axilla 98⅖°. Temp. rectum 100°. Pupils larger.	4.15	At 4.10 P. M. was drowsy, but would answer questions. Is now soundly asleep.
Pulse 104. Resp. 16. Axilla 98⅕°. Temp. rectum 99⅗°.	4.30	Respirations very deep, puffy, and full.
Pulse 92. Resp. 18. Axilla 98⅖°. Temp. rectum 99⅖°.	6	Still sleeping soundly.
Pulse 88. Resp. 18. Axilla 98⅖°. Temp. rectum 99⅖°. Pupils dilated, but not fixed.	7.15	Still asleep, but commences to be restless when touched during observation.

OBSERVATION 9.

J—— W——.

	A. M.	
Pulse 88. Resp. 20. Axilla 97⅕°. Temp. rectum 99⅖°. Pupils normal.	10.30	Quiet. Goes to bed without resistance and allows observations. Given ½ grain hyoscyamine by mouth.
Pulse 96. Resp. 20.	10.35.	
Pulse 124.	10.42.	Rapid, weak, indistinct.
Pulse 124. Resp. 18. Temp. rectum 99⅕°. Pupils dilating. Conjunctiva congested.	10.50	Respirations fuller and deeper. Commences to yawn. Begins to be very restless, but is drowsy.
Pulse 132.	10.55	Pulse very difficult to count. Patient very restless.
Pulse 116. Resp. 20. Temp. rectum 99⅕°. Pupils large.	11.10	Pulse improved in character.
Pulse 112. Resp. 22. Temp. rectum 99⅗°.	11.45	Seems inclined to sleep, but rouses very easily.

	P. M.	
Pulse 114. Resp 20. Temp. rectum 99⅘°.	1	Has slept a little. Not so restless. Lies with his eyes wide open and looks around in a drowsy manner.
Pulse 92. Resp. 20. Temp. rectum 100°.	2.30	Has not slept since last note. Rises up in bed on door being opened. Not so restless during observations. Conjunctiva not so red.
Pulse 92. Resp. 20. Temp. rectum 100°. Pupils still very large.	5.15	No tendency to sleep. Very little effect noticeable.

OBSERVATION 10.

J—— A——.

Chronic Mania.

	A. M.	
Pulse 60. Resp. 20. Axilla 98⅕°. Temp. rectum 99⅕°. Pupils normal.	10.50	Has been put to bed 20 minutes before observation. Slightly excited this morning, laughing and talking a great deal.

10.55 A. M., given ¼ grain hyoscyamine *hypodermically.*

	A. M.	
Pulse 92.	10.58	
Resp. 18.	11	Commences to feel sleepy, says his head is sore.
Pulse 100.	11.03	
Resp. 16	11.05	
Temp. rectum 99°.	11.08.	
Pulse 104.	11.10	Sound asleep. Will not speak. Pupils dilating. Conjunctiva injected.
Resp. 16.	11.12	Resp. full and deep. Patient snores.
Temp. axilla 98⅗°.	11.15	
Pulse 108.	11.18	
Resp. 18.	11.20	Snoring and blowing. Patient opens and shuts his eyes. Restless, rolls about the bed.
Pulse 108.	11.23	Pupils very large.

	A. M.	
Temp. rectum 98⅘°.	11.25	Tries to get up, but falls back in bed. Rubs his hands, knocks his head against the wall.
Pulse 120.	11.30	
Temp. axilla 98⅗°.	11.45	
Pulse 116.	11.50	Is asleep, but agitated. Tries to throw himself out of bed.
Temp. rectum 99⅖°.	11.55	
	M.	
Pulse 116.	12	
	P. M.	
Pulse 112. Resp. 20. Axilla 98⅖°. Temp. rectum 99⅗°. Pupils dilated.	12.30	Respiration blowing and snorting. Rolls out of bed on floor.
Pulse 92. Resp. 18. Axilla 98⅖°. Temp. rectum 99⅕°.	1	Sleeping quietly, but becomes restless during observation. Conjunctiva not so red.
Pulse 80. Resp. 16. Axilla 98⅕°. Temp. rectum 99°.	2	Sleeping soundly and snoring.
Pulse 76. Resp. 16. Axilla 98⅖°. Temp. rectum 99°.	3.30	Sleeping quietly. Gets out of bed and urinates, but afterward returns to bed.
Pulse 72. Resp. 16. Axilla 98⅘°. Temp. rectum 99°.	5	Still sleeping, but rouses easily. Refuses his supper.
Pulse 64. Resp. 18. Axilla 98°. Temp. rectum 98⅘. Pupils smaller.	7	Sleepy, but rouses easily and converses. Says his head aches. Pupils respond to candle light.

OBSERVATION II.

J—— L——.

Melancholia.

	P. M.	
Pulse 100. Resp. 26. Axilla 99⅕°. Temp. rectum 100°. Pupils normal.	2.30	Has been quiet all day. Makes no resistance to observations.

2.32 P. M., given $\frac{1}{6}$ grain hyoscyamine hypodermically.

		P. M.	
Pulse 96.		2.34	
" 92.		2.37	
" 96.		2.39	
" 104.		2.41	
" 112.		2.44	
" 116.		2.46	
" 118.		2.50	Pupils commencing to dilate.
Pulse 124.	Resp. 28.	2.55	Patient gets up in great anxiety. Says he is dying; that he feels dreadful. Asks for water and drinks it.
Pulse 150.		3	Tries to get up and falls back. Then embraces nurse with both arms. Moans, cries aloud, and says he is done.
Pulse 144.		3.20	
Pulse 136.	Resp. 28.	3.40	Tries to walk around but shuffles and stumbles. Tries to pick up clothes, but lets drop what he has in picking up a new piece. Violently resists temperature taking.
Pulse 132.	Resp. 28.	4	Quieter but still anxious. Has twice asked for a drink.
Pulse 116.	Resp. 26.	5	Has not slept, gets up and dresses. Will not allow temperature to be taken.
Pulse 80.	Resp. 30.	6.45	Is found sitting up in bed. Says he feels better, but has not slept any.

They were taken in persons of good physical health as far as flesh, etc., was concerned, and ranging from 20 to 40 years of age. We always placed the patient in bed, well covered up for half an hour before the first temperature was taken; after the first record of temperature then the medicine was given, still keeping the patient in bed until the end of the observation. Examination of the pulse rate shows that in eight cases it was increased in from five minutes to one hour and a half after the dose was taken.

The rule is first an increase in the number of pulse beats, to be followed by a diminution and return to the normal, occasionally to be followed by a slight diminution in the number of beats below the initial number. Sometimes there is at first a diminution in the number of pulse beats, soon to be followed by an increase in the number of pulsations much above the natural beats (in three of the eleven cases), then a gradual return to the normal. The respirations almost invariably are diminished in frequency, to be followed by a return to the normal. In the experiments on animals there was a slight increase in the respirations.

In eight cases in which the temperature was taken in the axilla, in five there was a slight fall in the temperature, and in three there was a slight rise; in one there was a slight fall, followed by a slight rise, and then a return to the normal.

In six cases there was a fall in the rectal temperature more or less marked, that is, from $\frac{1}{5}$ to 1 degree; in one case there was a slight fall and then a slight rise; in three cases there was a rise in temperature; in one of the cases the fall in temperature was followed by a decided rise.

In one of the first observations we made, the axillary temperature went up so much that we were led to inquire if the rise in the axillary temperature did not coincide with a fall in the rectal temperature, but further observation showed that whenever the axillary temperature falls the rectal also falls, when the axillary rises the rectal also rises; in one case only was there a rise in the axillary temperature and a fall in the rectal, and this was probably due to the patient's skin having been colder and registering below the normal; the precaution to cover them up well in bed for some time before taking the first observation and thereafter, avoided any error of this kind.

The dilatation of the pupil began and was at its height in from thirty minutes to one and a half hours, and the full dilatation was found to take place at about the time when the pulse rate was highest.

Our observations are entirely in accord with Gnauck's recently published researches on the following points: the tired, restless feeling (when the drug is first given there is sometimes a restless, uneasy state; the patient turns about in bed, puts his hands up to his face, rubs his eyes, etc.) coincides with the rise of the pulse rate, and the sleep always ensues with the fall of the pulse rate, when, as a rule, the patient sleeps quietly, and not unfrequently profoundly, and even snoring quite naturally.

The pupil which has been dilated with hyoscyamine we have found to become contracted during the sleep which ensues from the effect of the drug; that is, the pupil is less large during the sleep than it was during the waking state. Gnauck states that with the plithysmograph it was found that in the sleep from hyoscyamine the blood-vessels of the arm are dilated as in normal sleep. We have also found, as he has done, that the pupil dilated with hyoscyamine is not fixed, it will react to light—it does not contract down, as in a normal pupil, but it is mobile, and will contract to a certain degree; this was observed in the cases in which the drug was given internally as well as in those in which it was applied directly to the eye.

As regards its action on the pupil there is no question as to its mydriatic effect, but there appears to be some doubt as to its superiority or inferiority to atropia as a dilator of the pupil. In addition to the observations previously made with Dr. Ferris, in which the drug was given internally and the pupil noted, its local action was studied, observations were made in conjunction with my assistant, Dr. John Bowen. We first of all used a four-(4)-grain solution (4 grains to aqua ℥ i) of hyoscyamine and a four-(4)-grain solution of atropine, putting one drop of the hyoscyamine solution into the right eye, and a drop of atropine solution into the left eye. We found that the hyoscyamine eye began dilating first, but after a short time they were both dilated alike. This was the uniform result with the four-(4)-grain solution ; we then used a half-grain solution with the same result. We then tried a $\frac{1}{8}$-grain solution ; the hyoscyamine solution hardly dilated the pupil, while the atropine solution dilated them. The superiority of atropine over hyoscyamine as a mydriatic was well shown in the application of the weak solutions, whilst it was not apparent by the use of strong solutions ; its superiority was also shown by the persistence of the dilatation from atropine much longer than the dilatation from hyoscyamine. It was also noted in these observations, as in the previous ones with the internal administration of the alkaloid, that the pupils reacted to light—they were not fixed, as in the atropinized pupil. The other general effects of the alkaloid, when given to man, are : If the dose be large enough, a tottering, drunken kind of gait, with a rather drowsy, heavy expression ; soon the patient lies down, apparently unable to stand up any longer, and falls into a deep, quiet sleep, which lasts many hours. Occasionally the patient is restless, uneasy, and yet quite drowsy and partly asleep ; he rolls about in bed, rubs his face, etc., and later sleeps quietly if undisturbed.

The degree of profoundness in the sleep varies somewhat in different persons. In one of our observations we met with, to us, an unusual effect ; the patient was quite agitated, threw his arms around the doctor and nurse, said he was going to die, complained of dizziness, and evidently had a feeling of oppression ; pupils dilated and mouth very dry.

This is, however, an unusual condition and it appears to us that it may have been due to the man having been a melancholic.

The fauces are always more or less dry, its degree varying very much in different individuals.

Only occasionally is there a slight disposition to nausea; the appetite is not disturbed by it; delirium and hallucinations are rare, and are in no way to be compared with those seen in the use of atropia.

The urinary secretion is frequently increased. It has been my object in this article to avoid any discussion as to the therapeutics and antagonism of this alkaloid.

Most of the writers on this subject have been treating of the therapeutics of this alkaloid, and the physiological action has only been touched upon incidentally; without reviewing and comparing the observations of others with my own, I might say in closing that, as far as the physiological action of the drug is concerned, my observations are in the main in unison with those of Lawson, Mendal, Gnauck, and Seguin.

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